We claim:

1. A composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, which comprises a compound of the formula (I)

A-L-B (I)

in which

A is a monomer, multimer or polymer of TKPPR, or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B is a substrate.

2. A composition according to claim 1, wherein A is a multimer of TKPPR or a TKPPR analogue.

3. A composition according to claim 2, wherein A is a tetramer of TKPPR or a TKPPR analogue.

4. A composition according to claim 1, wherein B comprises

B_1, a lipid able to bind the linker in a covalent or non-covalent manner.

5. A composition according to claim 4, in which B_1 comprises a synthetic or naturally-occurring generally amphipathic and biocompatible compound, selected from the group consisting of fatty acids; lysolipids; phospholipids; phosphatidylinositol; sphingolipids; glycolipids; glucolipids; sulfatides; glycosphingolipids; phosphatidic acids; lipids bearing polymers; lipids bearing sulfonated mono- di-, oligo- or polysaccharides; cholesterol, cholesterol sulfate; cholesterol hemisuccinate; tocopherol hemisuccinate; lipids with ether and ester-linked fatty acids; polymerized lipids; diacetyl phosphate; dicetyl phosphate; stearylamine; cardiolipin; phospholipids with short chain fatty acids of about 6 to about 8 carbons in length; synthetic phospholipids with asymmetric acyl chains; ceramides; non-ionic liposomes; sterol esters of sugar acids; esters of sugars and aliphatic acids; saponins; glycerol dilaurate; glycerol trilaurate; glycerol dipalmitate; glycerol; glycerol esters; long chain alcohols; 6-(5-cholesten-3β-yloxy)-1-thio-β-D-galactopyranoside; digalactosyl-diglyceride; 6-(5-cholesten-3 β-yloxy)hexyl-6-amino-6-deoxy-1-thio-β-D-galacto-pyranoside; 6-(5-cholesten-3 β-yloxy)hexyl-6-amino-6-deoxyl-1-thio- βD-manno-

pyranoside; 12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)octadecanoic acid; N-[12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)octadecanoyl]-2-aminopalmitic acid; N-succinyldioleylphosphatidylethanolamine; 1,2-dioleyl-sn-glycerol; 1,2-dipalmitoyl-sn-3-succinylglycerol; 1,3-dipalmitoyl-2-succinylglycerol; 1-hexadecyl-2-palmitoylglycerophosphoethanolamine; palmitoylhomocysteine, and combinations thereof.

6. A composition according to claim 1, wherein B comprises
B_2, a non-lipid polymer able to bind the linker in a covalent manner.

7. A composition according to claim 6, in which B_2 comprises B_{2a} a polymer useful for producing microparticles, or B_{2b}, a non-ionic surfactant.

8. A composition according to claim 7 in which B_{2a} is selected from the group consisting of polyvinyl alcohol (PVA) and a polyoxyethylene-polyoxypropylene block copolymer.

9. A composition according to claim 7, in which B_{2a} comprises a bead which is derivatizable and is attached to a detectable label.

10. A composition according to claim 9, in which the detectable label is a fluorescent or radioactive marker.

11. A composition according to claim 1, in which B comprises a bioactive agent.

12. A composition according to claim 1, in which B comprises a delivery vehicle for genetic material.

13. A composition according to claim 1, in which B comprises a delivery vehicle for a drug or therapeutic.

14. A composition according to claim 1, in which B comprises Bc, a metal chelating group.

15. A composition according to claim 14, in which the metal chelating group is complexed with a metal.

16. A composition according to claim 15, in which the metal chelating group is complexed with a radioactive metal.

17. A composition according to claim 16, in which the metal chelating group is complexed with a radioactive metal useful for radiotherapy.

18. A composition according to claim 16, in which the metal chelating group is complexed with a radioactive metal useful for imaging.

19. A composition according to claim 16, in which the metal is selected from the group consisting of: ^{99m}Tc, ^{67}Ga, ^{68}Ga, ^{111}In, ^{88}Y, ^{90}Y, ^{105}Rh, ^{153}Sm, ^{166}Ho, ^{165}Dy, ^{177}Lu, ^{64}Cu, ^{97}Ru, ^{103}Ru, ^{186}Re, and ^{188}Re.

20. A composition according to claim 14, in which the metal chelating group Bc is selected from the list consisting of: N_4, S_4, N_3S, N_2S_2 and NS_3 chelators.

21. A composition according to claim 20, in which the metal chelating group Bc comprises oxa-PnAO.

22. A composition according to claim 21, in which A comprises a tetramer of TKPPR and the metal chelating group is complexed to ^{99m}Tc.

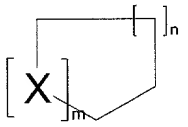
23. A composition according to claim 1, in which L is a bond or is derived from :

an alkyl chain C_1-C_{6000}, linear or branched, saturated or unsaturated, optionally interrupted or substituted by one or more groups such as: O, S, NR, OR, SR, COR, COOH, COOR, CONHR, CSNHR, C=O, S=O, $S(=O)_2$, $P=O(O)_2OR$, $P(O)_2(OR)_2$, halogens, or phenyl groups, optionally substituted by one or more -NHR, -OR, -SR, -COR, -CONHR, -N-C=S, -N-C=O, halogens, in which

R is H or an alkyl group C_1-C_4, linear or branched, optionally substituted by one or more –OH;

such a chain can be interrupted or substituted by one or more cyclic groups C_3-C_9, saturated or unsaturated, optionally interrupted by one or more O, S or NR; by one or more groups such as: -NHR, -OR, -SR, -COR, -CONHR, or a phenyl group optionally substituted by one or more -NHR, -OR, -SR, -COR, -CONHR, -N-C=S, -N-C=O, halogens.

24. A composition according to claim 23, in which the cyclic groups present in L are saturated or unsaturated, and correspond to the following general formula (III)



(III)

in which

n can range from 0 to 4;

m can range from 0 to 2;

X can be NH, NR, O, S or SR.

25. A composition according to claim 23, in which the linker L is an oligopeptide comprising 1 to 100 natural or synthetic amino acids.

26. A composition according to claim 25, in which the amino acids are selected from the group consisting of glycine, glutamic acid, aspartic acid, γ-amino-butyric acid and trans-4-aminomethyl-cyclohexane carboxylic acid.

27. A composition according to claim 23, in which L is derived from difunctional PEG-(polyethyleneglycol) derivatives.

28. A composition according to claim 23, in which L is selected from the group consisting of: glutaric acid, succinic acid, malonic acid, oxalic acid and PEG derivatized with two CH_2CO groups.

29. A compound of the formula (IIa) for use in targeting endothelial cells, tumor cells or other cells which express NP-1

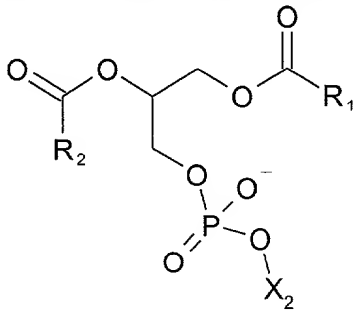
$$A\text{-}L\text{-}B_{1a} \quad \text{(IIa)}$$

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

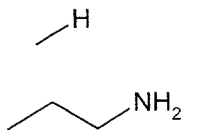
B_{1a} comprises a phospholipid moiety of the formula (II),



M (II)

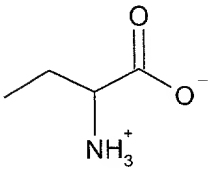
where

M	is an alkaline or alkaline- earth metal cation;
R_1 and R_2	independently, correspond to a linear long chain C_{12}-C_{20}; saturated or unsaturated, optionally interrupted by C=O, or O; and
X_2	is selected in a group consisting of

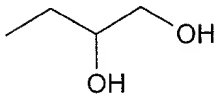


phosphatidic acid

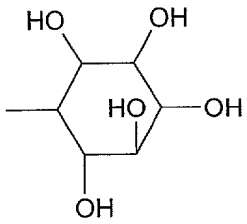
ethanolamine



serine



glycerol



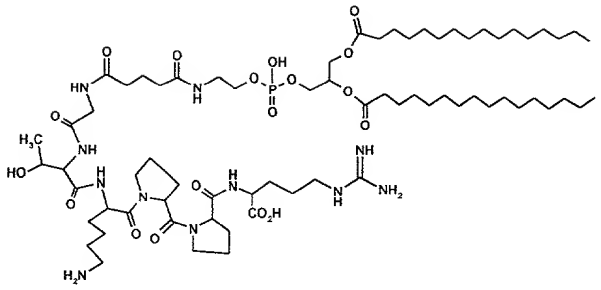
inositol

30. A compound according to claim 29, in which R_1 and R_2 are independently a saturated linear long chain C_{12}-C_{20}.

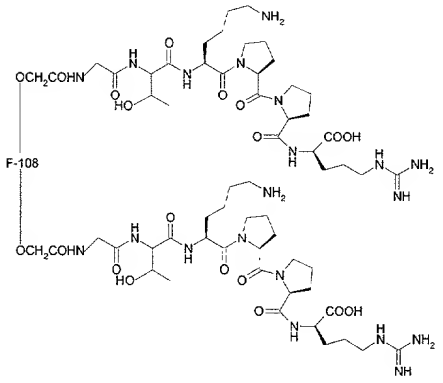
31. A compound according to claim 30, in which the phospholipid of formula (II) comprises a phospholipid selected from the group consisting of: dimyristoylphosphatidylethanolamine, dipalmitoylphosphatidylethanolamine, distearoylphosphatidylethanolamine, diarachidoylphosphatidylethanolamine, dioleylphosphatidylethanolamine, dilinoleylphosphatidylethanolamine, fluorinated analogues of any of the foregoing, and mixtures of any of the foregoing.

32. A compound according to claim 31, in which the phospholipid of formula (II) comprises dipalmitoylphosphatidylethanolamine.

33. A composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, comprising a compound selected from the group consisting of:



and



34. An ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of any one of claims 29 to 32.

35. An ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of claim 29 and the gas comprises a fluorinated gas.

36. An ultrasound contrast agent comprising a suspension of gas-filled microbubbles in which the microbubbles comprise a compound of claim 29 in which A is TKPPR tetramer and the gas comprises SF_6 or a perfluorocarbon selected from the group consisting of C_3F_8, C_4F_8, C_4F_{10}, C_5F_{12}, C_6F_{12}, C_7F_{14} and C_8F_{18}.

37. A compound for use in targeting endothelial cells, tumor cells or other cells that express NP-1 of the formula

$$A\text{-}L\text{-}B_3$$

where

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B_3 is a biodegradable, physiologically acceptable polymer.

38. An ultrasound contrast agent comprising a suspension of gas-filled microballoons, in which the microballoons comprise a compound of claim 37.

39. An ultrasound contrast agent comprising a suspension of gas-filled microballoons, in which the microballoons comprise a compound of claim 37 in which A is a TKPPR tetramer and the gas comprises a gas selected from the group consisting of: air; nitrogen; oxygen; CO_2; argon; xenon or krypton,a fluorinated gas, a low molecular weight hydrocarbon, an alkene or an alkyne and mixtures thereof.

40. A compound for use for use in targeting endothelial cells, tumor cells or other cells which express NP-1 comprising a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1or cells that express NP-1 with avidity that is equal to or greater than TKPPR.

41. A compound for use in inhibiting angiogenesis comprising a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR.

42. A pharmaceutical composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, comprising:

a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR; and

a pharmaceutically acceptable carrier.

43. A pharmaceutical composition for use in inhibiting angiogenesis comprising:

a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR; and

a pharmaceutically acceptable carrier.

44. A pharmaceutical composition for use in inhibiting angiogenesis comprising:

a tetramer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR; and

a pharmaceutically acceptable carrier.

45. A process for preparing a compound of claim 1 comprising:

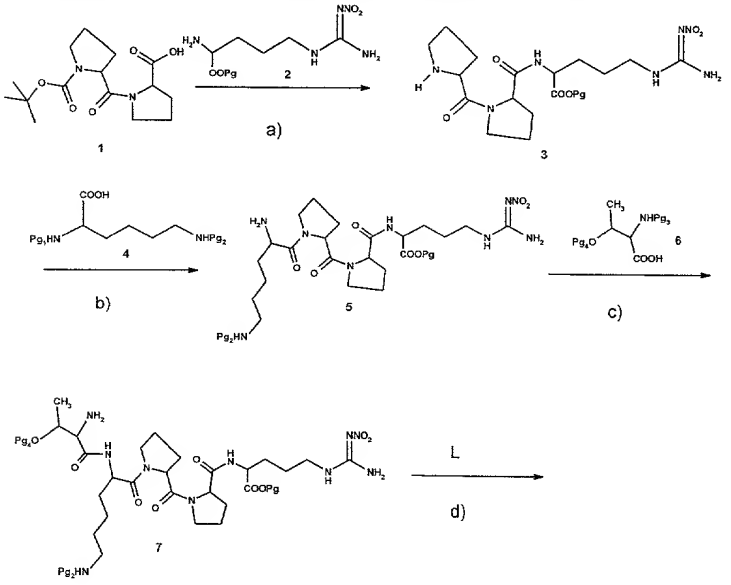
a) obtaining a monomer, multimer or polymer of TKPPR or an analogue thereof;

b) conjugating the monomer, multimer or polymer of TKPPR with the linker to give a compound of formula (IIb) ; and

A-L (IIb)

c) forming a covalent or non-covalent bond between a compound of formula (IIb) and the substrate B or forming a covalent bond between the substrate B and the linker to form a conjugate B-L, and
conjugating of the conjugate B-L with the monomer, multimer or polymer of TKPPR or an analogue thereof.

46. A process according to claim 45, in which the compounds of formula (IIb) are prepared as illustrated in the following Scheme



(Pg = protecting group)

in which

the steps a), b), and c) are all condensation reactions performed under basic conditions, and step d) is a condensation in basic conditions with the linker.

47. A method of imaging an angiogenic site in an human or animal comprising:

a) administering to said human or animal a composition comprising a compound of the formula (I)

A-L-B (I)

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells which express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B is a substrate, where B comprises a detectable moiety; and

b) detecting said moiety.

48. A method of imaging endothelial cells, tumor cells or other cells that express NP-1 in a human or animal comprising:

a) administering to said human or animal a composition comprising a compound of the formula (I)

A-L-B (I)

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells which express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B is a substrate, where B comprises a detectable moiety; and

b) detecting said moiety.

49. A method of ultrasound imaging comprising administering an ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of the formula (IIa)

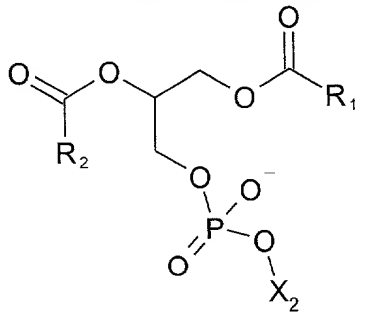
$A\text{-}L\text{-}B_{1a}$ (IIa)

in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells which express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B_{1a} comprises a phospholipid moiety of the formula (II),



M (II)

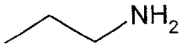
where

M is an alkaline or alkaline- earth metal cation;

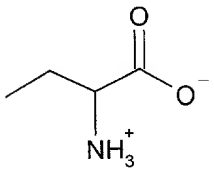
R_1 and R_2 independently, correspond to a linear long chain C_{12}-C_{20}; saturated or unsaturated, optionally interrupted by C=O, or O; and

X_2 is selected in a group consisting of

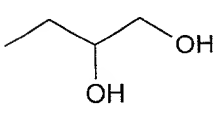
phosphatidic acid



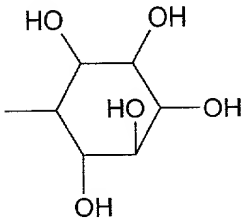
ethanolamine



serine



glycerol



inositol

50. A method of staging a tumor in a human or an animal comprising administering a composition comprising a detectable moiety and a compound of claim 1 to said human or animal and detecting said moiety in said human or animal.

51. A method of screening at least one agent for the ability of said agent to target endothelial cells, tumor cells or other cells that express NP-1, comprising contacting said cells in vitro with a composition of any one of claims 7 to 9.

52. A method of screening at least one targeted ultrasound contrast agent for the ability of said agent to target endothelial cells, tumor cells or other cells that express NP-1, comprising contacting said cells in vitro with a composition of any one of claims 7 to 9.

53. A method for the therapeutic delivery in vivo of a bioactive agent to a patient suffering from effects associated with angiogenesis-related disorders comprising administering a therapeutically effective amount of a composition of any one of claims 11 to 13.

54. A method of treating an individual exhibiting effects of an angiogenesis-related disorder comprising administering a therapeutically effective amount of a composition of any one of claims 11 to 13.

55. A composition according to claim 12, wherein B comprises a delivery vehicle for genetic material selected from the group consisting of: a virus particle, a viral or retroviral gene therapy vector, a liposome, a complex of cationic lipids and genetic material and a complex of dextran derivatives and genetic material.

56. A method for delivering desired nucleic acids to endothelial cells, tumor cells or other cells expressing NP-1, comprising administering a therapeutically effective amount of the composition of claim 55.

57. A method of enhancing endothelial cell-targeted gene therapy comprising incorporating compounds of claim 40 in or on the delivery vehicle for genetic material.

58. A method of enhancing tumor cell-targeted gene therapy comprising incorporating compounds of claim 40 in or on the delivery vehicle for genetic material.

59. A method of enhancing gene therapy targeting angiogenic cells comprising incorporating compounds of claim 41 in or on the delivery vehicle for genetic material.

60. A method for imaging of a human or animal comprising:

a) administering to said human or animal a composition according to any one of claims 16,18,19,21 or 22; and

b) imaging all or part of said human or animal using a camera that detects radiation.

61. A method for imaging of a human or animal comprising:

a) administering to said human or animal a composition according to claim 21; and

b) imaging all or part of said human or animal using a camera that detects radiation.

62. A method for treating a human or animal with a tumor or angiogenesis-related disease comprising administering to said human or animal a therapeutically effective amount of a composition according to either one of claims 17 or 19.

63. A kit for preparing a radiopharmaceutical comprising a composition of claim 14 or a pharmaceutically acceptable salt thereof.

64. A kit according to claim 63, further comprising an exchange ligand.

65. A kit according to either claim 63 or 64, further comprising a reducing agent.